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Opinion

Carcinogenicity, Mutagenicity and Cardiovascular risk: In silico evaluation of a novel COVID-19 therapy

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Introduction

The global pandemic of COVID-19, a highly contagious viral illness, is a major public health concern. Currently, the research community is seeking effective and safe pharmacotherapies. Paxlovid (Pox) is a combination of Nirmatrelvir (NR), a protease inhibitor, and Ritonavir (RT), which provides pharmacokinetic benefits. Due to the recent approval of Px, there is limited data regarding its safety and toxicological profile [1-3]. Thus, the objective of this paper is to evaluate the carcinogenic, mutagenic, and cardiovascular profiles of NR and RT by *in silico* prediction.

Materials and Methods: The toxic parameters were evaluated through PreADME software; AMES test and Rodent carcinogenicity assay. The positive results were confirmed by a Micronucleus assay.

Results and Discussion:

The predictions concerning the toxicological endpoints reveal that NR/RT can inhibit hERG, a potassium ion channel involved in normal cardiac repolarization activity of the heart. The drug-induced blockade of hERG function causes the long QT syndrome, which can result in arrhythmia and death. Although they did not cause mutation, these structures were classified as "ambiguous molecules" in the hERG adherence test. There is an uncertainty in ligand binding patterns within the central cavity of the canal and it must be further analyzed. The risk of channel inhibition creates a concomitant risk of cardiovascular side effects and sudden death [4,5].

In the Ames test, NR and RT were found to be non-mutagenic. NR has carcinogenic potential, while Rt has been shown not to be carcinogenic in mice. However, the use of Ritonavir is associated with hepatotoxicity and there is no specific antidote in case of overdose. In addition, Px can cause metabolic induction, increasing the risks of developing serious and potentially fatal adverse drug-related effects. [4]

Conclusion:

Both drugs may be associated with the increased risk of cardiovascular complications. Regarding mutagenicity, Px is relatively safe, considering the NR results. Patients in use of NR/RT should be monitored for drug toxicity and interactions. An interprofessional healthcare team can minimize the risk of harm and improve the patient's safety.

Thus, the development of bioinformatics techniques provides advances in several procedures for evaluating compounds and new drugs, ensuring the rational and respectful use of laboratory animals.

Keywords: anti-sars-cov-2 therapy; pharmaceutical chemistry; toxicology; bioinformatics

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